

1

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<110> Egelrud, Torbjorn
Hansson, Lennart

<120> SCCE modified transgenic mammals and
their use as models of human diseases

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Gly Pro Leu Val Cys Asn Asp
20

<210> 9

<211> 38

<212> PRT

<213> Bos taurus

<400> 9

Gln Glu Asp Gln Gly Asn Lys Ser Gly Glu Lys Ile Ile Asp Gly Val
1 5 10 15
Pro Cys Pro Arg Gly Ser Gln Pro Trp Gln Val Ala Leu Leu Lys Gly
20 25 30
Ser Gln Leu His Cys Gly
35

<210> 10

<211> 37

<212> PRT

<213> Sus scrofa

<400> 10

Gln Glu Gly Gln Asp Lys Ser Gly Glu Lys Ile Ile Asp Gly Val Pro
1 5 10 15
Cys Pro Gly Gly Ser Arg Pro Trp Gln Val Ala Leu Leu Lys Gly Asn
20 25 30
Gln L u His Cys Gly
35

<210> 11

<211> 34

<212> PRT

<213> Homo sapiens

<400> 11

Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp Gly Ala Pro Cys Ala Arg
1 5 10 15
Gly Ser His Pro Trp Gln Val Ala Leu Leu Ser Gly Asn Gln Leu His
20 25 30
Cys Gly

<210> 12

<211> 31

<212> PRT

<213> Rattus norvegicus

<400> 12

Gln Gly Glu Arg Ile Ile Asp Gly Tyr Lys Cys Lys Glu Gly Ser His
1 5 10 15
Pro Trp Gln Val Ala Leu Leu Lys Gly Asp Gln Leu His Cys Gly
20 25 30

8

<210> 13
<211> 31
<212> PRT
<213> Mus musculus

<400> 13
Gln Gly Glu Arg Ile Ile Asp Gly Ile Lys Cys Lys Glu Gly Ser His
1 5 10 15
Pro Trp Gln Val Ala Leu Leu Lys Gly Asn Gln Leu His Cys Gly
20 25 30

<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Consensus sequence for cleavage site in C-terminal
of SCCE.

<221> VARIANT
<222> 2
<223> Asp = either aspartate (Asp) or glutamate (Glu).

<221> VARIANT
<222> 3
<223> Lys = either lysine (Lys) or arginine (Arg).

<400> 14
Gly Asp Lys Ile Ile Asp Gly
1 5

<210> 15
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus of the substrate specificity pouch.

<221> VARIANT
<222> 1
<223> Thr = any amino acid residue.

<221> VARIANT
<222> 3
<223> Ala = any amino acid residue.

<221> VARIANT
<222> 5
<223> Asn = any amino acid residue.

<400> 15
Thr Asn Ala Cys Asn Gly Asp Ser
1 5

9

<210> 16
<211> 20
<212> DNA
<213> Artificial sequence

<220>
<223> PCR primer SYM3300.

<400> 16
ggtggccctg ctcaaggcca 20

<210> 17
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3301.

<400> 17
caccatggat gacacagcct gg 22

<210> 18
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3302.

<400> 18
aataaagaaa cacaaaaccc 20

<210> 19
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3418.

<400> 19
tgtaatatca ttgtgggc 18

<210> 20
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4118.

<400> 20
ggatgtgaag ctcatctc 18

<210> 21
<211> 18

10

<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4121.

<400> 21
tggagtcggg gatgccag

18

<210> 22
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4720.

<400> 22
gggaggggtgg agagagagtg cagtg

25

<210> 23
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4899.

<400> 23
agtctaggt gcagccccta c

21

<210> 24
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer hEXON1.

<400> 24
ctcgagggat ctgatgtgat cc

22

<210> 25
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mEXON1.

<400> 25
ctgggagtga cttggcgtgg ctct

24

<210> 26
<211> 23
<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer specific for human SCCE IE2.

<400> 26

gctctcccat tagtccccag aga

23

<210> 27

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer specific for human SCCE MJ2.

<400> 27

ccacttggtg aacttgcaca ctg

24

<210> 28

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> forward primer covering the position 427 - 444 of the human SCCE cDNA sequence.

<400> 28

gggaaccccc tggaacaa

18

<210> 29

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> reverse primer covering the position 490 - 510 of the human cDNA sequence in exon five.

<400> 29

acatccacgc acatgaggtc a

21

<210> 30

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> The real time amplification probe covering the position 445 - 473 of the human cDNA sequence in exon four.

<400> 30

cctgtactgt ctccggctgg ggcactacc

29

12

<210> 31
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mS3.

<400> 31
caaggagaaa ggattataga tggct 25

<210> 32
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 698.

<400> 32
aaggctccgc acccatggca g 21

<210> 33
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 696.

<400> 33
tgcaatggtg actcaggggg gccctt 26

<210> 34
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer H2.

<400> 34
gacccaggcg tctacactca agt 23

<210> 35
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mS4.

<400> 35
gagaccatga aaacccatcg ctaac 25

<210> 36

13

<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer KO 0905.

<400> 36
tgactttctt cacactggac gacagc 26

<210> 37
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer GR 0905.

<400> 37
ctcacactg gctgatagcc tggccg 26

<210> 38
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer Ngr.

<400> 38
cagggtggcg gaatgacctc atggccct 28

<210> 39
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer RA 1016.

<400> 39
ctactccaca aggacccatg tcaatgac 28

<210> 40
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer nRA 1016.

<400> 40
gctgtgtgct ggcattcccg actctaag 28

<210> 41
<211> 30

14

<212> DNA
<213> Artificial Sequence

<220>
<223> SMART II oligonucleotide.

<400> 41
aagcagtggg aacaacgcag agtacgcggg 30

<210> 42
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> 5'-RACE cDNA synthesis primer.

<221> variation
<222> 27
<223> n = a or g or c or t

<400> 42
ttttttttt ttttttttt tttttvn 27

<210> 43
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Long universal primer.

<400> 43
ctaatacgac tcactatagg gcaagcagt gtaacaacgc agagt 45

<210> 44
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Short universal primer.

<400> 44
ctaatacgac tcactatagg gcc 23

<210> 45
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Nested universal primer.

<400> 45
aagcagtggg aacaacgcag agt 23

<210> 46
<211> 243
<212> PRT

15

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
part of SCCE from cow.

<400> 46

```

Met Thr Thr Pro Leu Val Ile Leu Leu Leu Thr Phe Ala Leu Gly Ser
 1          5          10          15
Val Ala Gln Glu Asp Gln Gly Asn Lys Ser Gly Glu Lys Ile Ile Asp
          20          25          30
Gly Val Pro Cys Pro Arg Gly Ser Gln Pro Trp Gln Val Ala Leu Leu
          35          40          45
Lys Gly Ser Gln Leu His Cys Gly Gly Val Leu Leu Asn Glu Gln Trp
          50          55          60
Val Leu Thr Ala Ala His Cys Met Asn Glu Tyr Asn Val His Met Gly
65          70          75          80
Ser Val Arg Leu Val Gly Gly Gln Lys Ile Lys Ala Thr Arg Ser Phe
          85          90          95
Arg His Pro Gly Tyr Ser Thr Gln Thr His Ala Asn Asp Leu Met Leu
          100          105          110
Val Lys Leu Asn Gly Arg Ala Lys Leu Ser Ser Ser Val Lys Lys Val
          115          120          125
Asn Leu Pro Ser His Cys Asp Pro Pro Gly Thr Met Cys Thr Val Ser
          130          135          140
Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro Gly Gln Leu
145          150          155          160
Met Cys Thr Asp Val Lys Leu Ile Ser Pro Gln Asp Cys Arg Lys Val
          165          170          175
Tyr Lys Asp Leu Leu Gly Asp Ser Met Leu Cys Ala Gly Ile Pro Asn
          180          185          190
Ser Arg Thr Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro Leu Met Cys
          195          200          205
Lys Gly Thr Leu Gln Gly Val Val Ser Trp Gly Ser Phe Pro Cys Gly
          210          215          220
Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys Tyr Val Asn
225          230          235          240
Trp Ile Lys

```

<210> 47

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
part of SCCE from pig.

<400> 47

```

Met Ala Arg Pro Leu Leu Pro Pro Arg Leu Ile Leu Leu Ser Leu
 1          5          10          15
Ala Leu Gly Ser Ala Ala Gln Glu Gly Gln Asp Lys Ser Gly Glu Lys
          20          25          30
Ile Ile Asp Gly Val Pro Cys Pro Gly Gly Ser Arg Pro Trp Gln Val
          35          40          45
Ala Leu Leu Lys Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn
          50          55          60
Gln Gln Trp Val Leu Thr Ala Ala His Cys Met Met Asn Asp Tyr Asn
65          70          75          80

```

16

```

Val His Leu Gly Ser Asp Arg Leu Asp Asp Arg Lys Gly Gln Lys Ile
      85                      90                      95
Arg Ala Met Arg Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His
      100                    105                    110
Val Asn Asp Leu Met Leu Val Lys Leu Ser Arg Pro Ala Arg Leu Ser
      115                    120                    125
Ala Ser Val Lys Lys Val Asn Leu Pro Ser Arg Cys Glu Pro Pro Gly
      130                    135                    140
Thr Thr Cys Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val
      145                    150                    155                    160
Thr Phe Pro Ala Asp Leu Met Cys Thr Asp Val Lys Leu Ile Ser Ser
      165                    170                    175
Gln Asp Cys Lys Lys Val Tyr Lys Asp Leu Leu Gly Ser Ser Met Leu
      180                    185                    190
Cys Ala Gly Ile Pro Asn Ser Lys Thr Asn Ala Cys Asn Gly Asp Ser
      195                    200                    205
Gly Gly Pro Leu Val Cys Lys Gly Thr Leu Gln Gly Leu Val Ser Trp
      210                    215                    220
Gly Thr Phe Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln
      225                    230                    235                    240
Val Cys Lys Tyr Ile Asp Trp Ile Asn
      245

```

<210> 48

<211> 253

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
part of SCCE from homo.

<400> 48

```

Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
      5                      10                      15
Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
      20                    25                    30
Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
      35                    40                    45
Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
      50                    55                    60
Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
      65                    70                    75                    80
Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
      85                    90                    95
Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
      100                   105                   110
Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
      115                   120                   125
Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
      130                   135                   140
Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
      145                   150                   155                    160
Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
      165                   170                   175
Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
      180                   185                   190
Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
      195                   200                   205
Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe

```


17

210		215		220
Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys				
225		230		235
Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg				240
	245		250	

<210> 49
 <211> 226
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Deduced amino acid sequence from the C-terminal
 part of SCCE from rat.

<400> 49
 Met Gly Val Trp Leu Leu Ser Leu Leu Thr Val Leu Leu Ser Leu Ala
 1 5 10 15
 Leu Glu Thr Ala Gly Gln Gly Glu Arg Ile Ile Asp Gly Tyr Lys Cys
 20 25 30
 Lys Glu Gly Ser His Pro Trp Gln Val Ala Leu Leu Lys Gly Asp Gln
 35 40 45
 Leu His Cys Gly Gly Val Leu Val Gly Glu Ser Trp Val Leu Thr Ala
 50 55 60
 Ala His Cys Lys Met Gly Gln Tyr Thr Val His Leu Gly Ser Asp Lys
 65 70 75 80
 Ile Glu Asp Gln Ser Ala Gln Arg Ile Lys Ala Ser Arg Ser Phe Arg
 85 90 95
 His Pro Gly Tyr Ser Thr Arg Thr His Val Asn Asp Ile Met Leu Val
 100 105 110
 Lys Met Asp Lys Pro Val Lys Met Ser Asp Lys Val Gln Lys Val Lys
 115 120 125
 Leu Pro Asp His Cys Glu Pro Pro Gly Thr Leu Cys Thr Val Ser Gly
 130 135 140
 Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro Ser Asp Leu Met
 145 150 155 160
 Cys Ser Asp Val Lys Leu Ile Ser Ser Gln Glu Cys Lys Lys Val Tyr
 165 170 175
 Lys Asp Leu Leu Gly Lys Thr Met Leu Cys Ala Gly Ile Pro Asp Ser
 180 185 190
 Lys Thr Asn Thr Cys Asn Gly Asp Ser Gly Gly Pro Leu Val Cys Asn
 195 200 205
 Asp Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Tyr Pro Cys Gly Gln
 210 215 220
 Pro Asn
 225

<210> 50
 <211> 249
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Deduced amino acid sequence from the C-terminal
 part of SCCE from mouse.

<400> 50
 Met Gly Val Trp Leu Leu Ser Leu Ile Thr Val Leu Leu Ser Leu Ala
 1 5 10 15

18

Leu	Glu	Thr	Ala 20	Gly	Gln	Gly	Glu 25	Arg	Ile	Ile	Asp	Gly 30	Ile	Lys	Cys
Lys	Glu	Gly 35	Ser	His	Pro	Trp	Gln 40	Val	Ala	Leu	Leu	Lys 45	Gly	Asn	Gln
Leu	His 50	Cys	Gly	Gly	Val	Leu 55	Val	Asp	Lys	Tyr	Trp 60	Val	Leu	Thr	Ala
Ala 65	His	Cys	Lys	Met	Gly 70	Gln	Tyr	Gln	Val	Gln	Leu	Gly 75	Ser	Asp	Lys 80
Ile	Gly	Asp	Gln	Ser 85	Ala	Gln	Lys	Ile	Lys 90	Ala	Thr	Lys	Ser	Phe	Arg
His	Pro	Gly	Tyr 100	Ser	Thr	Lys	Thr	His 105	Val	Asn	Asp	Ile	Met 110	Leu	Val
Arg	Leu	Asp 115	Glu	Pro	Val	Lys	Met 120	Ser	Ser	Lys	Val	Glu 125	Ala	Val	Gln
Leu	Pro 130	Glu	His	Cys	Glu	Pro 135	Pro	Gly	Thr	Ser	Cys 140	Thr	Val	Ser	Gly
Trp 145	Gly	Thr	Thr	Thr	Ser 150	Pro	Asp	Val	Thr	Phe 155	Pro	Ser	Asp	Leu	Met 160
Cys	Ser	Asp	Val	Lys 165	Leu	Ile	Ser	Ser	Arg 170	Glu	Cys	Lys	Lys	Val	Tyr
Lys	Asp	Leu 180	Leu	Gly	Lys	Thr	Met 185	Leu	Cys	Ala	Gly	Ile 190	Pro	Asp	Ser
Lys	Thr	Asn 195	Thr	Cys	Asn	Gly	Asp 200	Ser	Gly	Gly	Pro	Leu 205	Val	Cys	Asn
Asp	Thr 210	Leu	Gln	Gly	Leu	Ala 215	Ser	Arg	Gly	Thr	Tyr 220	Pro	Cys	Gly	Gln
Pro 225	Asn	Asp	Pro	Gly	Val 230	Tyr	Thr	Gln	Val	Cys 235	Lys	Tyr	Lys	Arg	Trp 240
Val	Met	Glu	Thr	Met 245	Lys	Thr	His	Arg							